

CLAIMS

What is claimed is:

1. A method of preventing organ ischemia or reperfusion injury comprising administering to a living subject in need thereof a pharmaceutical composition comprising:
 - a. a serine protease inhibitor; and
 - b. adenosine, an adenosine agonist or a pharmaceutically acceptable derivative or prodrug or metabolite thereof.
2. The method of claim 1, wherein the serine protease inhibitor is selected from the group consisting of 4-(2-aminoethyl) benzenesulfonylfluoride, α -amino-*n*-caproic acid, α_1 -antichymotrypsin, antipain, antithrombin III, α_1 -antitrypsin, *p*-amidinophenylmethyl sulfonyl fluoride, aprotinin, cathepsin/subtilisin inhibitor (Boc-Val-Phe-NHO-Bz-*p*Cl), chymostatin ([(*S*)-1-carboxy-2-phenylethyl]-carbamoyl- α -[2-amidohexahydro-4(*S*)-pyrimidyl]-(*S*)-glycyl-[A = Leu, B = Val, or C = Ile]-phenylalaninal), chymotrypsin inhibitor I, 3,4-dichloroisocoumarin, diisopropylfluoro phosphate, dipeptidylpeptidase IV inhibitor I (Ile-Pro-Ile), dipeptidylpeptidase IV inhibitor II (H-Glu-(NHO-Bz)-Pyr), ecotin, elastase inhibitor I (Boc-Ala-Ala-Ala-NHO-Bz), α_2 -macroglobulin, PPACK (*D*-Phe-Pro-Arg-chloromethylketone), PPACK II, *N*^α-tosyl-Lys chloromethyl ketone, *N*^α-tosyl-Phe chloromethyl ketone, and any mixture thereof.
3. The method of claim 1, wherein the adenosine agonist or pharmaceutically acceptable derivative is selected from the group consisting of AB-MECA (*N*⁶-4-aminobenzyl-5'-*N*-methyl carboxamidoadenosine), CPA (*N*⁶-cyclopentyladenosine), ADAC (*N*⁶-[4-[[[4-[[[(2-aminoethyl) amino] carbonyl] methyl]-anilino] carbonyl] methyl] phenyl] adenosine), CCPA (2-chloro-*N*⁶-cyclopentyladenosine), CHA (*N*⁶-cyclohexyladenosine), GR79236 (*N*⁶-[1*S*, *trans*,2-hydroxy cyclopentyl] adenosine), *S*-ENBA ((2*S*)- *N*⁶-(2-endonorbanyl)adenosine), IAB-MECA (*N*⁶-(4-amino-3-iodobenzyl)adenosine-5'-*N*-methylcarboxamidoadenosine), *R*-PIA (*R*-*N*⁶-(phenyl isopropyl) adenosine), ATL146e (4-{3-[6-amino-9-(5-ethylcarbamoyl-3,4-dihydroxy-

tetrahydro-furan-2-yl)-9H-purin-2-yl]-prop-2-ynyl}-cyclohexanecarboxylic acid methyl ester), CGS-21680 (APEC or 2-[*p*-(2-carbonyl-ethyl)-phenyl ethyl amino]-5'-*N*-ethylcarboxamidoadenosine), CV1808 (2-phenylaminoadenosine), HENECA (2-hex-1-ynyl-5'-*N*-ethylcarboxamido adenosine), NECA (5'-*N*-ethyl-carboxamido adenosine), PAPA-APEC (2-(4-[2-[(4-aminophenyl) methyl carbonyl] ethyl] phenyl) ethylamino-5'-*N*-ethyl carboxamidoadenosine), DITC-APEC (2-[*p*-(4-isothiocyanatophenylamino thiocarbonyl-2-ethyl)-phenylethylamino]-5'-*N*-ethylcarboxamido adenosine), DPMA (*N*⁶-(2(3,5-dimethoxy phenyl)-2-(2-methyl phenyl) ethyl)adenosine), *S*-PHPNECA ((*S*)-2-phenylhydroxypropynyl-5'-*N*-ethylcarbox amidoadenosine), WRC-0470 (2-cyclohexylmethylidenhydrazinoadenosine), AMP-579 (1*S*-[1a,2b,3b,4a(*S*^{*})])]-4-[7-[[2-(3-chloro-2-thienyl)-1-methylpropyl]amino]-3H-imidazo [4,5-*b*] pyridyl-3-yl] cyclopentane carboxamide), IB-MECA (*N*⁶- (3-iodobenzyl) adenosine -5'-*N*-methyluronamide), 2-ClADO (2-chloroadenosine), I-ABA (*N*⁶-(4-amino-3-iodobenzyl)adenosine), *S*-PIA (*S*-*N*⁶-(phenylisopropyl) adenosine), 2-[(2-aminoethyl-aminocarbonyl)ethyl] phenylethyl amino]-5'-*N*-ethyl-carboxamido adenosine, 2-Cl-IB-MECA (2-chloro-*N*⁶- (3-iodobenzyl)adenosine-5'-*N*-methyluronamide), polyadenylic acid, and any mixture thereof.

4. A pharmaceutical composition comprising:
 - a. a serine protease inhibitor; and
 - b. adenosine, an adenosine agonist or a pharmaceutically acceptable derivative or prodrug or metabolite thereof.
5. The pharmaceutical composition of claim 4, wherein the serine protease inhibitor is selected from the group consisting of 4-(2-aminoethyl) benzenesulfonylfluoride, α -amino-*n*-caproic acid, α_1 -antichymotrypsin, antipain, antithrombin III, α_1 -antitrypsin, *p*-amidino phenylmethylsulfonyl fluoride, aprotinin, cathepsin/subtilisin inhibitor (Boc-Val-Phe-NHO-Bz-*p*Cl), chymostatin ([(*S*)-1-carboxy-2-phenylethyl]-carbamoyl- α - [2-amidohexahydro-4(*S*)-pyrimidyl]-(*S*)-glycyl-[A = Leu, B = Val, or C = Ile]-phenyl alaninal), chymotrypsin inhibitor I, 3,4-dichloroisocoumarin,

diisopropylfluorophosphate, dipeptidylpeptidase IV inhibitor I (Ile-Pro-Ile), dipeptidylpeptidase IV inhibitor II (H-Glu-(NHO-Bz)-Pyr), ecotin, elastase inhibitor I (Boc-Ala-Ala-Ala-NHO-Bz), α_2 -macroglobulin, PPACK (*D*-Phe-Pro-Arg-chloromethylketone), PPACK II, *N*^a-tosyl-Lys chloromethyl ketone, *N*^a-tosyl-Phe chloromethyl ketone, and any mixture thereof.

6. The pharmaceutical composition of claim 4, wherein the adenosine agonist or pharmaceutically acceptable derivative is selected from the group consisting of AB-MECA (*N*⁶-4-aminobenzyl-5'-*N*-methylcarboxamido adenosine), CPA (*N*⁶-cyclopentyladenosine), ADAC (*N*⁶-[4-[[[4-[[[(2-aminoethyl) amino] carbonyl] methyl]-anilino] carbonyl] methyl] phenyl] adenosine), CCPA (2-chloro-*N*⁶-cyclopentyl adenosine), CHA (*N*⁶-cyclohexyladenosine), GR79236 (*N*⁶-[1*S*, *trans*,2-hydroxy cyclopentyl] adenosine), *S*-ENBA ((2*S*)-*N*⁶-(2-endonorbanyl) adenosine), IAB-MECA (*N*⁶-(4-amino-3-iodobenzyl)adenosine-5'-*N*-methylcarboxamido adenosine), *R*-PIA (*R*-*N*⁶-(phenylisopropyl) adenosine), ATL146e (4-{3-[6-amino-9-(5-ethyl carbamoyl-3,4-dihydroxy-tetrahydro-furan-2-yl)-9H-purin-2-yl]-prop-2-ynyl}-cyclohexane carboxylic acid methyl ester), CGS-21680 (APEC or 2-[*p*-(2-carbonyl-ethyl)-phenyl ethyl amino]-5'-*N*-ethylcarboxamido adenosine), CV1808 (2-phenylamino adenosine), HENECA (2-hex-1-ynyl-5'-*N*-ethylcarboxamido adenosine), NECA (5'-*N*-ethyl-carboxamido adenosine), PAPA-APEC (2-(4-[2-[(4-aminophenyl)methylcarbonyl]ethyl] phenyl) ethylamino-5'-*N*-ethyl carboxamido adenosine), DITC-APEC (2-[*p*-(4-isothiocyanatophenylamino thiocarbonyl-2-ethyl)-phenylethylamino]-5'-*N*-ethylcarboxamido adenosine), DPMA (*N*⁶-(2(3,5-dimethoxy phenyl)-2-(2-methylphenyl)ethyl)adenosine), *S*-PHPNECA ((*S*)-2-phenylhydroxypropynyl-5'-*N*-ethylcarboxamido adenosine), WRC-0470 (2-cyclohexyl methylidenehydrazino adenosine), AMP-579 (1*S*-[1*a*,2*b*,3*b*,4*a*(*S*^{*})]-4-[7-[[2-(3-chloro-2-thienyl)-1-methylpropyl]amino]-3H-imidazo [4,5-*b*] pyridyl-3-yl] cyclopentane carboxamide), IB-MECA (*N*⁶- (3-iodobenzyl)adenosine-5'-*N*-methyluronamide), 2-CIADO (2-chloroadenosine), I-ABA (*N*⁶-(4-amino-3-iodobenzyl) adenosine), *S*-PIA (*S*-*N*⁶-(phenylisopropyl)adenosine), 2-[(2-

aminoethyl-aminocarbonyl ethyl) phenylethyl amino]-5'-*N*-ethyl-carboxamidoadenosine, 2-Cl-IB-MECA (2-chloro-*N*⁶-(3-iodobenzyl) adenosine-5'-*N*-methyluronamide), polyadenylic acid, and any mixture thereof.

7. A method of preventing organ ischemia or reperfusion injury comprising concomitantly administering to a living subject in need thereof
 - a. a serine protease inhibitor; and
 - b. adenosine, an adenosine agonist or a pharmaceutically acceptable derivative or prodrug or metabolite thereof.
8. The method of claim 7, wherein the serine protease inhibitor is selected from the group consisting of 4-(2-aminoethyl) benzenesulfonyl fluoride, α -amino-*n*-caproic acid, α_1 -antichymotrypsin, antipain, antithrombin III, α_1 -antitrypsin, *p*-amidinophenylmethyl sulfonyl fluoride, aprotinin, cathepsin/subtilisin inhibitor (Boc-Val-Phe-NHO-Bz-*p*Cl), chymostatin ([(*S*)-1-carboxy-2-phenylethyl]-carbamoyl- α -[2-amidohexahydro-4-(*S*)-pyrimidyl]-(*S*)-glycyl-[A = Leu, B = Val, or C = Ile]-phenylalaninal), chymotrypsin inhibitor I, 3,4-dichloroisocoumarin, diisopropylfluorophosphate, dipeptidylpeptidase IV inhibitor I (Ile-Pro-Ile), dipeptidylpeptidase IV inhibitor II (H-Glu-(NHO-Bz)-Pyr), ecotin, elastase inhibitor I (Boc-Ala-Ala-Ala-NHO-Bz), α_2 -macroglobulin, PPACK (*D*-Phe-Pro-Arg-chloromethylketone), PPACK II, *N* ^{α} -tosyl-Lys.chloromethyl ketone, *N* ^{α} -tosyl-Phe chloromethyl ketone, and any mixture thereof.
9. The method of claim 7, wherein the adenosine agonist or pharmaceutically acceptable derivative is selected from the group consisting of AB-MECA (*N*⁶-4-aminobenzyl-5'-*N*-methylcarboxamidoadenosine), CPA (*N*⁶-cyclopentyladenosine), ADAC (*N*⁶-[4-[[[4-[[[(2-aminoethyl) amino] carbonyl] methyl]-anilino] carbonyl] methyl] phenyl] adenosine), CCPA (2-chloro-*N*⁶-cyclopentyladenosine), CHA (*N*⁶-cyclohexyladenosine), GR79236 (*N*⁶-[1*S*, *trans*,2-hydroxycyclopentyl] adenosine), *S*-ENBA ((2*S*)-*N*⁶-(2-endonorbanyl)adenosine), IAB-MECA (*N*⁶-(4-amino-3-iodobenzyl)adenosine-5'-*N*-methylcarboxamidoadenosine), *R*-PIA (*R*-*N*⁶-(phenylisopropyl)

adenosine), ATL146e (4-{3-[6-amino-9-(5-ethylcarbamoyl-3,4-dihydroxy-tetrahydro-furan-2-yl)-9H-purin-2-yl]-prop-2-ynyl}-cyclohexanecarboxylic acid methyl ester), CGS-21680 (APEC or 2-[*p*-(2-carbonyl-ethyl)-phenyl ethyl amino]-5'-*N*-ethylcarboxamido adenosine), CV1808 (2-phenylaminoadenosine), HENECA (2-hex-1-ynyl-5'-*N*-ethylcarboxamido adenosine), NECA (5'-*N*-ethyl-carboxamido adenosine), PAPA-APEC (2-(4-[2-[(4-amino phenyl) methylcarbonyl]ethyl] phenyl) ethylamino-5'-*N*-ethyl carboxamidoadenosine), DITC-APEC (2-[*p*-(4-isothiocyanatophenylamino thiocarbonyl-2-ethyl)-phenylethylamino]-5'-*N*-ethylcarboxamidoadenosine), DPMA (*N*⁶-(2(3,5-dimethoxy phenyl)-2-(2-methylphenyl)ethyl)adenosine), *S*-PHPNECA ((*S*)-2-phenylhydroxypropynyl-5'-*N*-ethylcarboxamidoadenosine), WRC-0470 (2-cyclohexylmethylidenehydrazinoadenosine), AMP-579 (1*S*-[1a,2b,3b,4a(*S*^{*})]-4-[7-[[2-(3-chloro-2-thienyl)-1-methylpropyl]amino]-3H-imidazo [4,5-*b*] pyridyl-3-yl] cyclo pentane carboxamide), IB-MECA (*N*⁶-(3-iodobenzyl)adenosine-5'-*N*-methyluronamide), 2-ClADO (2-chloroadenosine), I-ABA (*N*⁶-(4-amino-3-iodobenzyl) adenosine), *S*-PIA (*S*-*N*⁶-(phenylisopropyl)adenosine), 2-[(2-aminoethyl-aminocarbonyl)ethyl] phenylethyl amino]-5'-*N*-ethyl-carboxamidoadenosine, 2-Cl-IB-MECA (2-chloro-*N*⁶-(3-iodobenzyl)adenosine-5'-*N*-methyluronamide), polyadenylic acid, and any mixture thereof.

10. A method of preventing organ ischemia or reperfusion injury comprising administering to a living subject in need thereof sequentially in any order
 - a. a serine protease inhibitor; and
 - b. adenosine, an adenosine agonist or a pharmaceutically acceptable derivative or prodrug or metabolite thereof.
11. The method of claim 10, wherein the serine protease inhibitor is selected from the group consisting of 4-(2-aminoethyl) benzenesulfonylfluoride, α -amino-*n*-caproic acid, α ₁-antichymotrypsin, antipain, antithrombin III, α ₁-antitrypsin, *p*-amidinophenylmethyl sulfonyl fluoride, aprotinin, cathepsin/subtilisin inhibitor (Boc-Val-Phe-NHO-Bz-*p*Cl), chymostatin ([(*S*)-1-carboxy-2-phenylethyl]-carbamoyl- α -[2-amidohexahydro-4(*S*)-pyrimidyl]-(*S*)-glycyl-[A

= Leu, B = Val, or C = Ile]-phenylalaninal), chymotrypsin inhibitor I, 3,4-dichloroisocoumarin, diisopropylfluorophosphate, dipeptidylpeptidase IV inhibitor I (Ile-Pro-Ile), dipeptidylpeptidase IV inhibitor II (H-Glu-(NHO-Bz)-Pyr), ecotin, elastase inhibitor I (Boc-Ala-Ala-Ala-NHO-Bz), α_2 -macroglobulin, PPACK (*D*-Phe-Pro-Arg-chloromethylketone), PPACK II, *N*²-tosyl-Lys chloromethyl ketone, *N*²-tosyl-Phe chloromethyl ketone, and any mixture thereof.

12. The method of claim 10, wherein the adenosine agonist or pharmaceutically acceptable derivative is selected from the group consisting of AB-MECA (*N*⁶-4-aminobenzyl-5'-*N*-methylcarboxamidoadenosine), CPA (*N*⁶-cyclopentyladenosine), ADAC (*N*⁶-[4-[[[4-[[[(2-aminoethyl) amino] carbonyl] methyl]-anilino] carbonyl] methyl] phenyl] adenosine), CCPA (2-chloro-*N*⁶-cyclopentyladenosine), CHA (*N*⁶-cyclohexyladenosine), GR79236 (*N*⁶-[1*S*, *trans*,2-hydroxycyclopentyl] adenosine), *S*-ENBA ((2*S*)-*N*⁶-(2-endonorbanyl)adenosine), IAB-MECA (*N*⁶-(4-amino-3-iodobenzyl)adenosine-5'-*N*-methylcarboxamidoadenosine), *R*-PIA (*R*-*N*⁶-(phenylisopropyl)adenosine), ATL146e (4-{3-[6-amino-9-(5-ethylcarbonyl-3,4-dihydroxy-tetrahydro-furan-2-yl)-9H-purin-2-yl]-prop-2-ynyl}-cyclohexanecarboxylic acid methyl ester), CGS-21680 (APEC or 2-[*p*-(2-carbonyl-ethyl)-phenyl ethyl amino]-5'-*N*-ethylcarbox amido adenosine), CV1808 (2-phenylaminoadenosine), HENECA (2-hex-1-ynyl-5'-*N*-ethylcarboxamido adenosine), NECA (5'-*N*-ethyl-carboxamido adenosine), PAPA-APEC (2-(4-[2-[(4-amino phenyl) methylcarbonyl]ethyl] phenyl) ethylamino-5'-*N*-ethyl carboxamidoadenosine), DITC-APEC (2-[*p*-(4-isothiocyanatophenylamino thiocarbonyl-2-ethyl)-phenylethylamino]-5'-*N*-ethylcarboxamidoadenosine), DPMA (*N*⁶-(2(3,5-dimethoxy phenyl)-2-(2-methylphenyl)ethyl) adenosine), *S*-PHPNECA ((*S*)-2-phenylhydroxypropynyl-5'-*N*-ethylcarboxamidoadenosine), WRC-0470 (2-cyclohexylmethylidenehydrazinoadenosine), AMP-579 (1*S*-[1*a*,2*b*,3*b*,4*a*(*S*^{*})]-4-[7-[[2-(3-chloro-2-thienyl)-1-methylpropyl]amino]-3H-imidazo [4,5-*b*] pyridyl-3-yl] cyclo pentane carboxamide), IB-MECA (*N*⁶- (3-iodobenzyl)adenosine-5'-*N*-methyluronamide), 2-ClADO (2-chloroadenosine),

I-ABA (*N*⁶-(4-amino-3-iodobenzyl) adenosine), *S*-PIA (*S*-*N*⁶-(phenylisopropyl)adenosine), 2-[(2-aminoethyl-aminocarbonylethyl) phenylethyl amino]-5'-*N*-ethyl-carboxamidoadenosine, 2-Cl-IB-MECA (2-chloro-*N*⁶-(3-iodobenzyl)adenosine-5'-*N*-methyluronamide), polyadenylic acid, and any mixture thereof.

13. A method of preventing organ or tissue injury at a predetermined point or period of intervention comprising administering to a living subject in need thereof a pharmaceutical composition comprising:
 - a. a serine protease inhibitor; and
 - b. adenosine, an adenosine agonist or a pharmaceutically acceptable derivative or prodrug or metabolite thereof.
14. The method of claim 13, wherein the organ or tissue injury is related to at least one of cardiac surgery, non-surgical cardiac revascularization, organ transplantation, perfusion, ischemia, reperfusion, ischemia-reperfusion injury, oxidant injury, cytokine induced injury, shock induced injury, resuscitations injury, and apoptosis.
15. The method of claim 13, wherein the administering is taken at the predetermined point of intervention related to at least one of pre-treatment regimen, pharmacological preconditioning, reperfusion, or post interventional therapy, wherein the pharmacological preconditioning is a treatment administered before the ischemic intervention followed by a brief period of reperfusion or washout.
16. The method of claim 13, wherein the serine protease inhibitor is selected from the group consisting of 4-(2-aminoethyl) benzenesulfonylfluoride, α -amino-*n*-caproic acid, α_1 -antichymotrypsin, antipain, antithrombin III, α_1 -antitrypsin, *p*-amidinophenylmethyl sulfonyl fluoride, aprotinin, cathepsin/subtilisin inhibitor (Boc-Val-Phe-NHO-Bz-*p*Cl), chymostatin ([*(S)*-1-carboxy-2-phenylethyl]-carbamoyl- α -[2-amidohexahydro-4(*S*)-pyrimidyl]-(*S*)-glycyl-[A = Leu, B = Val, or C = Ile]-phenylalaninal), chymotrypsin inhibitor I, 3,4-dichloroisocoumarin, diisopropylfluorophosphate, dipeptidylpeptidase IV inhibitor I (Ile-Pro-Ile), dipeptidylpeptidase IV inhibitor II (H-Glu-(NHO-Bz)-

Pyr), ecotin, elastase inhibitor I (Boc-Ala-Ala-Ala-NHO-Bz), α_2 -macroglobulin, PPACK (*D*-Phe-Pro-Arg-chloromethylketone), PPACK II, N^{α} -tosyl-Lys chloromethyl ketone, N^{α} -tosyl-Phe chloromethyl ketone, and any mixture thereof.

17. The method of claim 13, wherein the adenosine agonist or pharmaceutically acceptable derivative is selected from the group consisting of AB-MECA (N^6 -4-aminobenzyl-5'-*N*-methylcarboxamidoadenosine), CPA (N^6 -cyclopentyladenosine), ADAC (N^6 -[4-[[[4-[[[(2-aminoethyl) amino] carbonyl] methyl]-anilino] carbonyl] methyl] phenyl] adenosine), CCPA (2-chloro- N^6 -cyclopentyladenosine), CHA (N^6 -cyclohexyladenosine), GR79236 (N^6 -[1*S*, *trans*,2-hydroxycyclopentyl] adenosine), *S*-ENBA ((2*S*)- N^6 -(2-endonorbanyl)adenosine), IAB-MECA (N^6 -(4-amino-3-iodobenzyl)adenosine-5'-*N*-methylcarboxamidoadenosine), *R*-PIA (*R*- N^6 -(phenylisopropyl)adenosine), ATL146e (4-{3-[6-amino-9-(5-ethylcarbamoyl-3,4-dihydroxy-tetrahydro-furan-2-yl)-9H-purin-2-yl]-prop-2-ynyl}-cyclohexanecarboxylic acid methyl ester), CGS-21680 (APEC or 2-[*p*-(2-carbonyl-ethyl)-phenyl ethyl amino]-5'-*N*-ethylcarboxamidoadenosine), CV1808 (2-phenylaminoadenosine), HENECA (2-hex-1-ynyl-5'-*N*-ethylcarboxamido adenosine), NECA (5'-*N*-ethyl-carboxamido adenosine), PAPA-APEC (2-(4-[2-[(4-aminophenyl) methyl carbonyl]ethyl] phenyl) ethylamino-5'-*N*-ethyl carboxamidoadenosine), DITC-APEC (2-[*p*-(4-isothiocyanatophenylamino thiocarbonyl-2-ethyl)-phenylethylamino]-5'-*N*-ethylcarboxamidoadenosine), DPMA (N^6 -(2(3,5-dimethoxy phenyl)-2-(2-methyl phenyl) ethyl)adenosine), *S*-PHPNECA ((*S*)-2-phenylhydroxypropynyl-5'-*N*-ethyl carboxamidoadenosine), WRC-0470 (2-cyclohexylmethylidenehydrazinoadenosine), AMP-579 (1*S*-[1a,2b,3b,4a(*S**)]]-4-[7-[[2-(3-chloro-2-thienyl)-1-methylpropyl]amino]-3H-imidazo [4,5-*b*] pyridyl-3-yl] cyclopentane carboxamide), IB-MECA (N^6 -(3-iodo benzyl)adenosine-5'-*N*-methyluronamide), 2-CIADO (2-chloroadenosine), I-ABA (N^6 -(4-amino-3-iodobenzyl) adenosine), *S*-PIA (*S*- N^6 -(phenylisopropyl)adenosine), 2-[(2-amino ethyl-aminocarbonyl)ethyl]

phenylethyl amino]-5'-*N*-ethyl-carboxamidoadenosine, 2-Cl-IB-MECA (2-chloro-*N*⁶-(3-iodobenzyl)adenosine-5'-*N*-methyluronamide), polyadenylic acid, and any mixture thereof.

18. A method of preventing organ ischemia or reperfusion injury comprising administering to a living subject in need thereof a pharmaceutical composition comprising:
 - a. a protease inhibitor; and
 - b. an agent that alters activities of G protein coupled receptors and cAMP, an analog or a pharmaceutically acceptable derivative or prodrug or metabolite thereof.
19. The method of claim 18, wherein the protease inhibitor is selected from the group consisting of 4-(2-aminoethyl) benzenesulfonylfluoride, α -amino-*n*-caproic acid, α_1 -antichymotrypsin, antipain, antithrombin III, α_1 -antitrypsin, *p*-amidinophenylmethyl sulfonyl fluoride, aprotinin, cathepsin/subtilisin inhibitor (Boc-Val-Phe-NHO-Bz-*p*Cl), chymostatin ([(*S*)-1-carboxy-2-phenylethyl]-carbamoyl- α -[2-amidohexahydro-4(*S*)-pyrimidyl]-(*S*)-glycyl-[A = Leu, B = Val, or C = Ile]-phenylalaninal), chymotrypsin inhibitor I, 3,4-dichloroisocoumarin, diisopropylfluoro phosphate, dipeptidylpeptidase IV inhibitor I (Ile-Pro-Ile), dipeptidylpeptidase IV inhibitor II (H-Glu-(NHO-Bz)-Pyr), ecotin, elastase inhibitor I (Boc-Ala-Ala-Ala-NHO-Bz), α_2 -macroglobulin, PPACK (*D*-Phe-Pro-Arg-chloromethylketone), PPACK II, *N*^α-tosyl-Lys chloromethyl ketone, *N*^α-tosyl-Phe chloromethyl ketone, acetyl-pepstatin (Ac-Val-Val-(3*S*,4*S*)-Sta-Ala-(3*S*,4*S*)-Sta-OH), calpain inhibitor I (*N*-acetyl-Leu-Leu-norleucinal), calpain inhibitor II (*N*-acetyl-Leu-Leu-Met-CHO), amastatin ([(*2S*, *2R*)]-3-amino-2-hydroxy-5-methylhexanoyl]-Val-Val-Asp-OH), arphamenine A ((*2R*,*5S*)-5-amino-8-guanidino-4-oxo-2-phenylmethyl octanoic acid), arphamenine B ((*2R*,*5S*)-5-amino-8-guanidino-4-oxo-2-*p*-hydroxyphenyl methyloctanoic acid), benzamidine, bestatin ([(*2S*, *2R*)-3-amino-2-hydroxy-4-phenyl butanoyl]-*L*-Leucine), CA-074 ((*L*-3-*trans*-[propylcarbamoyl]oxirane-2-carbonyl)-*L*-isoleucyl-*L*-proline), CA-074-Me ((*L*-3-*trans*-[propylcarbamoyl]oxirane-2-carbonyl)-*L*-isoleucyl-*L*-proline-

methylester), calpastatin, calpeptin (benzyloxycarbonylleucyl-norleucinal), carboxypeptidase inhibitor, cathepsin inhibitor I (Z-Phe-Gly-NHO-Bz), cathepsin inhibitor II (Z-Phe-Gly-NHO-Bz-*p*Me), cathepsin inhibitor III (Z-Phe-Gly-NHO-Bz-*p*OMe), cathepsin B inhibitor I (Z-Phe-Ala-CH₂F), cathepsin B inhibitor II (Ac-Leu-Val-lysinal), cathepsin L inhibitor I (Z-Phe-Phe-CH₂F), cathepsin L inhibitor II (Z-Phe-Tyr-CHO), cathepsin L inhibitor III (Z-Phe-Tyr-(*t*-Bu)-CHN₂), cathepsin L inhibitor IV (1-naphthalenesulfonyl-Ile-Trp-CHO), cathepsin L inhibitor V (Z-Phe-Tyr(O*t*Bu)-COCHO), cathepsin L inhibitor VI (*N*-(4-biphenylacetyl)-*S*-methylcysteine-(*D*)-Arg-Phe- \square -phenethylamide), cathepsin S inhibitor (Z-Phe-Leu-COCHO), cystatin, diprotin A (H-Ile-Pro-Ile-OH), E-64 (*trans*-epoxysuccinyl-*L*-leucylamido-(4-guanidino)butane), E-64 d (loxistatin, or (2*S*,3*S*)-*trans*-epoxysuccinyl-*L*-leucylamido-3-methylbutane ethyl ester), ebelactone A (3,11-dihydroxy-2,4,6,8,10,12-hexamethyl-9-oxo-6-tetradecenoic 1,3-lactone), ebelactone B (2-ethyl-3,11-dihydroxy-4,6,8,10,12-penta methyl -9-oxo-6-tetradecenoic 1,3-lactone), EDTA (ethylenediamine tetraacetic acid), EGTA (ethyleneglycol-*bis*(\square -aminoethyl)-*N,N,N',N'*-tetraacetic acid), elastase inhibitor II (MeOSuc-Ala-Ala-Pro-Ala-CMK), elastase inhibitor III (MeOSuc-Ala-Ala-Pro-Val-CMK), elastatinal (Leu-(Cap)-Gln-Ala-al or *N*-[(*S*)-1-carboxy-isopentyl]-carbamoyl- α -(2-iminohexahydro-4(*S*)-pyrimidyl]-*L*-glycyl-*L*-glutaminy-*L*-alaninal), E-64 (*trans*-epoxysuccinyl-*L*-leucylamido-(4-guanidino)butane), E-64 d (loxistatin, or (2*S*,3*S*)-*trans*-epoxysuccinyl-*L*-leucylamido-3-methylbutane ethyl ester), *N*-ethyl maleimide, GGACK (1,5-dansyl-*L*-glutamyl-*L*-glycyl-*L*-arginine chloromethyl ketone), galardin (*N*-[(2*S*)-(methoxycarbonylmethyl)-4-methylpentanoyl]-*L*-tryptophan-methyl amide), 2-guanidinoethylmercaptosuccinic acid, hirudin, HIV protease inhibitor (Ac-Leu-Val-phenylalaninal), leuhistin (((2*R*,3*S*)-3-amino-2-hydroxy-2-(1H-imidazol-4-ylmethyl)-5-methyl)-5-methylhexanoic acid), leupeptin (acetyl-leucyl-leucyl-arginal), NCO-700, PEFABLOC SC (4-(2-aminoethyl)-benzenesulfonyl fluoride), pepstatin (isovaleryl-Val-Val-4-amino-3-hydroxy-

6-methylheptanoyl-Ala-4-amino-3-hydroxy-6-methylheptanoic acid), phebestin ((2*S*,3*R*)-3-amino-2-hydroxy-4-phenylbutanoyl-*L*-valyl-*L*-phenylalanine), PMSF (phenyl methyl sulfonyl fluoride), phosphoramidon (*N*-alpha-*L*-rhamnopyranosyloxy(hydroxyl phosphinyl)-*L*-Leucyl-*L*-tryptophan, plummer's inhibitor (*D,L*-2-mercaptomethyl-3-guanidino-ethylthiopropionic acid), 1,10-phenanthroline, subtilisin inhibitor I (Boc-Ala-Ala-NHO-Bz), subtilisin inhibitor II (Z-Gly-Phe-NHO-Bz), subtilisin inhibitor III (Z-Gly-Phe-NHO-Bz-*p*OMe), subtilisin inhibitor IV (Boc-Pro-Phe-NHO-Bz-*p*Cl), subtilisin inhibitor V (Boc-Ala-Pro-Phe-NHO-Bz), TIMP-2 (tissue inhibitor of metalloproteinase 2), trypsin inhibitor, secretory leukocyte protease inhibitor, and any mixture thereof.

20. The method of claim 18, wherein the agent that alters activities of G protein coupled receptors and cAMP or pharmaceutically acceptable derivative is selected from the group consisting of AB-MECA (*N*⁶-4-aminobenzyl-5'-*N*-methylcarboxamidoadenosine), CPA (*N*⁶-cyclopentyladenosine), ADAC (*N*⁶-[4-[[[4-[[[(2-aminoethyl) amino] carbonyl] methyl]-anilino] carbonyl] methyl] phenyl] adenosine), CCPA (2-chloro-*N*⁶-cyclopentyl adenosine), CHA (*N*⁶-cyclohexyladenosine), GR79236 (*N*⁶-[1*S*, *trans*,2-hydroxycyclopentyl] adenosine), *S*-ENBA ((2*S*)- *N*⁶-(2-endonorbanyl)adenosine), IAB-MECA (*N*⁶-(4-amino-3-iodobenzyl)adenosine-5'-*N*-methylcarboxamidoadenosine), *R*-PIA (*R*-*N*⁶-(phenyl isopropyl) adenosine), ATL146e (4-{3-[6-amino-9-(5-ethylcarbamoyl-3,4-dihydroxy-tetrahydro-furan-2-yl)-9H-purin-2-yl]-prop-2-ynyl}-cyclohexanecarboxylic acid methyl ester), CGS-21680 (APEC or 2-[*p*-(2-carbonyl-ethyl)-phenyl ethyl amino]-5'-*N*-ethylcarboxamidoadenosine), CV1808 (2-phenylaminoadenosine), HENECA (2-hex-1-ynyl-5'-*N*-ethylcarboxamido adenosine), NECA (5'-*N*-ethyl-carboxamido adenosine), PAPA-APEC (2-(4-[2-[(4-aminophenyl)methylcarbonyl]ethyl] phenyl) ethylamino-5'-*N*-ethyl carboxamidoadenosine), DITC-APEC (2-[*p*-(4-isothiocyanatophenylamino thio carbonyl-2-ethyl)-phenylethylamino]-5'-*N*-ethylcarboxamidoadenosine), DPMA (*N*⁶-(2(3,5-dimethoxy phenyl)-2-(2-methylphenyl)ethyl)adenosine), *S*-PHPNECA ((*S*)-2-phenylhydroxypropynyl-

5'-*N*-ethylcarboxamidoadenosine), WRC-0470 (2-cyclohexyl methylidenehydrazinoadenosine), AMP-579 (1*S*-[1*a*,2*b*,3*b*,4*a*(*S*^{*})]-4-[7-[[2-(3-chloro-2-thienyl)-1-methylpropyl]amino]-3*H*-imidazo [4,5-*b*] pyridyl-3-yl] cyclopentane carboxamide), IB-MECA (*N*⁶- (3-iodobenzyl)adenosine-5'-*N*-methyluronamide), 2-CIADO (2-chloroadenosine), I-ABA (*N*⁶-(4-amino-3-iodobenzyl) adenosine), *S*-PIA (*S*-*N*⁶-(phenylisopropyl)adenosine), 2-[(2-aminoethyl-aminocarbonyl)ethyl] phenylethyl amino]-5'-*N*-ethyl-carboxamidoadenosine, 2-Cl-IB-MECA (2-chloro-*N*⁶- (3-iodobenzyl) adenosine-5'-*N*-methyluronamide), adenosine, polyadenylic acid, and any mixture thereof.

21. A pharmaceutical composition comprising:
 - a. a protease inhibitor; and
 - b. an agent that alters activities of G protein coupled receptors and cAMP or a pharmaceutically acceptable derivative or prodrug thereof.
22. The pharmaceutical composition of claim 21, wherein the protease inhibitor is selected from the group consisting of 4-(2-aminoethyl) benzenesulfonylfluoride, α -amino-*n*-caproic acid, α_1 -antichymotrypsin, antipain, antithrombin III, α_1 -antitrypsin, *p*-amidinophenylmethyl sulfonyl fluoride, aprotinin, cathepsin/subtilisin inhibitor (Boc-Val-Phe-NHO-Bz-*p*Cl), chymostatin ([(*S*)-1-carboxy-2-phenylethyl]-carbamoyl- α - [2-amidohexahydro-4(*S*)-pyrimidyl]-(*S*)-glycyl-[A = Leu, B = Val, or C = Ile]-phenylalaninal), chymotrypsin inhibitor I, 3,4-dichloroisocoumarin, diisopropylfluoro phosphate, dipeptidylpeptidase IV inhibitor I (Ile-Pro-Ile), dipeptidylpeptidase IV inhibitor II (H-Glu-(NHO-Bz)-Pyr), ecotin, elastase inhibitor I (Boc-Ala-Ala-Ala-NHO-Bz), α_2 -macroglobulin, PPACK (*D*-Phe-Pro-Arg-chloromethylketone), PPACK II, *N* ^{α} -tosyl-Lys chloromethyl ketone, *N* ^{α} -tosyl-Phe chloromethyl ketone, acetyl-pepstatin (Ac-Val-Val-(3*S*,4*S*)-Sta-Ala-(3*S*,4*S*)-Sta-OH), calpain inhibitor I (*N*-acetyl-Leu-Leu-norleucinal), calpain inhibitor II (*N*-acetyl -Leu-Leu-Met-CHO), amastatin ([2*S*, 2*R*]-3-amino-2-hydroxy-5-methylhexanoyl] -Val-Val-Asp-OH), arphamenine A ((2*R*,5*S*)-5-amino-8-guanidino-4-oxo-2-phenylmethyl octanoic acid),

arphamenine B ((2*R*,5*S*)-5-amino-8-guanidino-4-oxo-2-*p*-hydroxyphenyl
 methyloctanoic acid), benzamidine, bestatin ([[(2*S*, 2*R*)-3-amino-2-hydroxy-4-
 phenyl butanoyl] -*L*-Leucine), CA-074 ((*L*-3-*trans*-[propylcarbamoyl]oxirane-
 2-carbonyl)-*L*-isoleucyl-*L*-proline), CA-074-Me ((*L*-3-*trans*-
 [propylcarbamoyl]oxirane-2-carbonyl)-*L*-isoleucyl-*L*-proline-methylester),
 calpastatin, calpeptin (benzyloxycarbonylleucyl-norleucinal),
 carboxypeptidase inhibitor, cathepsin inhibitor I (Z-Phe-Gly-NHO-Bz),
 cathepsin inhibitor II (Z-Phe-Gly-NHO-Bz-*p*Me), cathepsin inhibitor III (Z-
 Phe-Gly-NHO-Bz-*p*OMe), cathepsin B inhibitor I (Z-Phe-Ala-CH₂F),
 cathepsin B inhibitor II (Ac-Leu-Val-lysinal), cathepsin L inhibitor I (Z-Phe-
 Phe- CH₂F), cathepsin L inhibitor II (Z-Phe-Tyr-CHO), cathepsin L inhibitor
 III (Z-Phe-Tyr-(*t*-Bu)-CHN₂), cathepsin L inhibitor IV (1-
 naphthalenesulfonyl-Ile-Trp-CHO), cathepsin L inhibitor V (Z-Phe-
 Tyr(OrBu)-COCHO), cathepsin L inhibitor VI (*N*-(4-biphenylacetyl)-*S*-
 methylcysteine-(*D*)-Arg-Phe-□-phenethylamide), cathepsin S inhibitor (Z-
 Phe-Leu-COCHO), cystatin, diprotin A (H-Ile-Pro-Ile-OH), E-64 (*trans*-
 epoxysuccinyl-*L*-leucylamido-(4-guanidino)butane), E-64 d (loxistatin, or
 (2*S*,3*S*)-*trans*-epoxysuccinyl-*L*-leucylamido-3-methylbutane ethyl ester),
 ebelactone A (3,11-dihydroxy-2,4,6,8,10,12-hexamethyl-9-oxo-6-
 tetradecenoic 1,3-lactone), ebelactone B (2-ethyl-3,11-dihydroxy-4,6,8,10,12-
 penta methyl -9-oxo-6-tetradecenoic 1,3-lactone), EDTA (ethylenediamine
 tetraacetic acid), EGTA (ethyleneglycol-*bis*(□-aminoethyl)-*N,N,N',N'*-
 tetraacetic acid), elastase inhibitor II (MeOSuc-Ala-Ala-Pro-Ala-CMK),
 elastase inhibitor III (MeOSuc-Ala-Ala-Pro-Val-CMK), elastatinal (Leu-
 (Cap)-Gln-Ala-al or *N*-[(*S*)-1-carboxy-isopentyl]-carbamoyl-α-(2-
 iminohexahydro-4(*S*)-pyrimidyl]-*L*-glycyl-*L*-glutaminy-*L*-alaninal), E-64
 (*trans*-epoxysuccinyl-*L*-leucylamido-(4-guanidino)butane), E-64d (loxistatin,
 or (2*S*,3*S*)-*trans*-epoxysuccinyl-*L*-leucylamido-3-methylbutane ethyl ester), *N*-
 ethyl maleimide, GGACK (1,5-dansyl-*L*-glutamyl-*L*-glycyl-*L*-arginine chloro
 methyl ketone), galardin (*N*-[(2*S*)-(methoxycarbonylmethyl)-4-
 methylpentanoyl]-*L*-tryptophan-methyl amide), 2-

guanidinoethylmercaptosuccinic acid, hirudin, HIV protease inhibitor (Ac-Leu-Val-phenylalaninal), leuhistin (((2*R*,3*S*)-3-amino-2-hydroxy-2-(1*H*-imidazol-4-ylmethyl)-5-methyl)-5-methylhexanoic acid), leupeptin (acetyl-leucyl-leucyl-arginal), NCO-700, PEFABLOC SC (4-(2-aminoethyl)-benzenesulfonyl fluoride), pepstatin (isovaleryl-Val-Val-4-amino-3-hydroxy-6-methylheptanoyl-Ala-4-amino-3-hydroxy-6-methylheptanoic acid), phebestin ((2*S*,3*R*)-3-amino-2-hydroxy-4-phenylbutanoyl-*L*-valyl-*L*-phenylalanine), PMSF (phenyl methyl sulfonyl fluoride), phosphoramidon (*N*-alpha-*L*-rhamnopyranosyloxy(hydroxyl phosphinyl)-*L*-Leucyl-*L*-tryptophan, plummer's inhibitor (*D,L*-2-mercaptomethyl-3-guanidino-ethylthiopropionic acid), 1,10-phenanthroline, subtilisin inhibitor I (Boc-Ala-Ala-NHO-Bz), subtilisin inhibitor II (Z-Gly-Phe-NHO-Bz), subtilisin inhibitor III (Z-Gly-Phe-NHO-Bz-*p*OMe), subtilisin inhibitor IV (Boc-Pro-Phe-NHO-Bz-*p*Cl), subtilisin inhibitor V (Boc-Ala-Pro-Phe-NHO-Bz), TIMP-2 (tissue inhibitor of metalloproteinase 2), trypsin inhibitor, secretory leukocyte protease inhibitor, and any mixture thereof.

23. The pharmaceutical composition of claim 21, wherein the agent that alters activities of G protein coupled receptors and cAMP or pharmaceutically acceptable derivative is selected from the group consisting of AB-MECA (*N*⁶-4-aminobenzyl-5'-*N*-methylcarboxamidoadenosine), CPA (*N*⁶-cyclopentyladenosine), ADAC (*N*⁶-[4-[[[4-[[[(2-aminoethyl) amino] carbonyl] methyl]-anilino] carbonyl] methyl] phenyl] adenosine), CCPA (2-chloro-*N*⁶-cyclopentyladenosine), CHA (*N*⁶-cyclohexyladenosine), GR79236 (*N*⁶-[1*S*, *trans*,2-hydroxycyclopentyl] adenosine), *S*-ENBA ((2*S*)- *N*⁶-(2-endonorbanyl)adenosine), IAB-MECA (*N*⁶-(4-amino-3-iodobenzyl)adenosine-5'-*N*-methylcarboxamidoadenosine), *R*-PIA (*R*-*N*⁶-(phenylisopropyl)adenosine), ATL146e (4-{3-[6-amino-9-(5-ethyl carbamoyl -3,4-dihydroxy-tetrahydro-furan-2-yl)-9H-purin-2-yl]-prop-2-ynyl}-cyclohexanecarboxylic acid methyl ester), CGS-21680 (APEC or 2-[*p*-(2-carbonyl-ethyl)-phenyl ethyl amino]-5'-*N*-ethylcarboxamidoadenosine), CV1808 (2-phenylamino adenosine), HENECA (2-hex-1-ynyl-5'-*N*-ethylcarboxamido adenosine),

NECA (5'-*N*-ethyl-carboxamido adenosine), PAPA-APEC (2-(4-[2-[(4-aminophenyl)methylcarbonyl] ethyl] phenyl) ethylamino-5'-*N*-ethyl carboxamido adenosine), DITC-APEC (2-[*p*-(4-isothiocyanatophenylamino thiocarbonyl-2-ethyl)-phenylethylamino]-5'-*N*-ethylcarbox amido adenosine), DPMA (*N*⁶-(2(3,5-dimethoxy phenyl)-2-(2-methylphenyl)ethyl) adenosine), *S*-PHPNECA ((*S*)-2-phenylhydroxypropynyl-5'-*N*-ethylcarboxamido adenosine), WRC-0470 (2-cyclohexylmethylidenehydrazino adenosine), AMP-579 (1*S*-[1a,2b,3b,4a(*S**)])]-4-[7-[2-(3-chloro-2-thienyl)-1-methylpropyl]amino]-3H-imidazo [4,5-*b*] pyridyl-3-yl] cyclopentane carboxamide), IB-MECA (*N*⁶- (3-iodobenzyl) adenosine -5'-*N*-methyluronamide), 2-CIADO (2-chloroadenosine), I-ABA (*N*⁶-(4-amino-3-iodobenzyl) adenosine), *S*-PIA (*S*-*N*⁶-(phenylisopropyl)adenosine), 2-[(2-aminoethyl-aminocarbonyl ethyl) phenylethyl amino]-5'-*N*-ethyl-carboxamido adenosine, 2-Cl-IB-MECA (2-chloro-*N*⁶- (3-iodobenzyl)adenosine-5'-*N*-methyluronamide), adenosine, polyadenylic acid, and any mixture thereof.

24. A method of preventing organ ischemia or reperfusion injury comprising concomitantly administering to a living subject in need thereof
 - a. a protease inhibitor; and
 - b. an agent that alters activities of G protein coupled receptors and cAMP or a pharmaceutically acceptable derivative or prodrug thereof.
25. The method of claim 24, wherein the protease inhibitor is selected from the group consisting of 4-(2-aminoethyl) benzenesulfonyl fluoride, α -amino-*n*-caproic acid, α_1 -antichymotrypsin, antipain, antithrombin III, α_1 -antitrypsin, *p*-amidinophenylmethyl sulfonyl fluoride, aprotinin, cathepsin/subtilisin inhibitor (Boc-Val-Phe-NHO-Bz-*p*Cl), chymostatin ([(*S*)-1-carboxy-2-phenylethyl]-carbamoyl- α - [2-amidohexahydro-4(*S*)-pyrimidyl]-(*S*)-glycyl-[A = Leu, B = Val, or C = Ile]-phenylalaninal), chymotrypsin inhibitor I, 3,4-dichloroisocoumarin, diisopropylfluoro phosphate, dipeptidylpeptidase IV inhibitor I (Ile-Pro-Ile), dipeptidylpeptidase IV inhibitor II (H-Glu-(NHO-Bz)-Pyr), ecotin, elastase inhibitor I (Boc-Ala-Ala-Ala-NHO-Bz), α_2 -

macroglobulin, PPACK (*D*-Phe-Pro-Arg-chloromethylketone), PPACK II, *N*^α-tosyl-Lys chloromethyl ketone, *N*^α-tosyl-Phe chloromethyl ketone, acetyl-pepstatin (Ac-Val-Val-(3*S*,4*S*)-Sta-Ala-(3*S*,4*S*)-Sta-OH), calpain inhibitor I (*N*-acetyl-Leu-Leu-norleucinal), calpain inhibitor II (*N*-acetyl-Leu-Leu-Met-CHO), amastatin ([*(2S, 2R)*]-3-amino-2-hydroxy-5-methylhexanoyl]-Val-Val-Asp-OH), arphamenine A (*(2R,5S)*-5-amino-8-guanidino-4-oxo-2-phenylmethyl octanoic acid), arphamenine B (*(2R,5S)*-5-amino-8-guanidino-4-oxo-2-*p*-hydroxyphenyl methyl octanoic acid), benzamidine, bestatin ([*(2S, 2R)*]-3-amino-2-hydroxy-4-phenyl butanoyl]-*L*-Leucine), CA-074 (*(L-3-trans*-[propylcarbamoyl]oxirane-2-carbonyl)-*L*-isoleucyl-*L*-proline), CA-074-Me (*(L-3-trans*-[propylcarbamoyl]oxirane-2-carbonyl)-*L*-isoleucyl-*L*-proline-methylester), calpastatin, calpeptin (benzyloxycarbonylleucyl-norleucinal), carboxypeptidase inhibitor, cathepsin inhibitor I (Z-Phe-Gly-NHO-Bz), cathepsin inhibitor II (Z-Phe-Gly-NHO-Bz-*p*Me), cathepsin inhibitor III (Z-Phe-Gly-NHO-Bz-*p*OMe), cathepsin B inhibitor I (Z-Phe-Ala-CH₂F), cathepsin B inhibitor II (Ac-Leu-Val-lysinal), cathepsin L inhibitor I (Z-Phe-Phe-CH₂F), cathepsin L inhibitor II (Z-Phe-Tyr-CHO), cathepsin L inhibitor III (Z-Phe-Tyr-(*t*-Bu)-CHN₂), cathepsin L inhibitor IV (1-naphthalenesulfonyl-Ile-Trp-CHO), cathepsin L inhibitor V (Z-Phe-Tyr(O*t*Bu)-COCHO), cathepsin L inhibitor VI (*N*-(4-biphenylacetyl)-*S*-methylcysteine-(*D*)-Arg-Phe-□-phenethylamide), cathepsin S inhibitor (Z-Phe-Leu-COCHO), cystatin, diprotin A (H-Ile-Pro-Ile-OH), E-64 (*trans*-epoxysuccinyl-*L*-leucylamido-(4-guanidino)butane), E-64 d (loxistatin, or *(2S,3S)*-*trans*-epoxysuccinyl-*L*-leucylamido-3-methylbutane ethyl ester), ebelactone A (3,11-dihydroxy-2,4,6,8,10,12-hexamethyl-9-oxo-6-tetradecenoic 1,3-lactone), ebelactone B (2-ethyl-3,11-dihydroxy-4,6,8,10,12-penta methyl -9-oxo-6-tetradecenoic 1,3-lactone), EDTA (ethylenediamine tetraacetic acid), EGTA (ethyleneglycol-*bis*(□-aminoethyl)-*N,N,N',N'*-tetraacetic acid), elastase inhibitor II (MeOSuc-Ala-Ala-Pro-Ala-CMK), elastase inhibitor III (MeOSuc-Ala-Ala-Pro-Val-CMK), elastatinal (Leu-(Cap)-Gln-Ala-al or *N*-[(*S*)-1-carboxy-isopentyl]-carbamoyl-α-(2-

iminohexahydro-4(*S*)-pyrimidyl]-*L*-glycyl-*L*-glutaminyl-*L*-alaninal), E-64 (*trans*-epoxysuccinyl-*L*-leucylamido-(4-guanidino)butane), E-64d (loxistatin, or (2*S*,3*S*)-*trans*-epoxysuccinyl-*L*-leucylamido-3-methylbutane ethyl ester), *N*-ethyl maleimide, GGACK (1,5-dansyl-*L*-glutamyl-*L*-glycyl-*L*-arginine chloro methyl ketone), galaridin (*N*-[(2*S*)-(methoxycarbonylmethyl)-4-methylpentanoyl]-*L*-tryptophan-methyl amide), 2-guanidinoethylmercaptosuccinic acid, hirudin, HIV protease inhibitor (Ac-Leu-Val-phenylalaninal), leuhistin (((2*R*,3*S*)-3-amino-2-hydroxy-2-(1*H*-imidazol-4-ylmethyl)-5-methyl)-5-methylhexanoic acid), leupeptin (acetyl-leucyl-leucyl-arginal), NCO-700, PEFABLOC SC (4-(2-aminoethyl)-benzenesulfonyl fluoride), pepstatin (isovaleryl-Val-Val-4-amino-3-hydroxy-6-methylheptanoyl-Ala-4-amino-3-hydroxy-6-methylheptanoic acid), phebestin ((2*S*,3*R*)-3-amino-2-hydroxy-4-phenylbutanoyl-*L*-valyl-*L*-phenylalanine), PMSF (phenyl methyl sulfonyl fluoride), phosphoramidon (*N*-alpha-*L*-rhamnopyranosyloxy(hydroxyl phosphinyl)-*L*-Leucyl-*L*-tryptophan, plummer's inhibitor (*D,L*-2-mercaptomethyl-3-guanidino-ethylthiopropionic acid), 1,10-phenanthroline, subtilisin inhibitor I (Boc-Ala-Ala-NHO-Bz), subtilisin inhibitor II (Z-Gly-Phe-NHO-Bz), subtilisin inhibitor III (Z-Gly-Phe-NHO-Bz-*p*OMe), subtilisin inhibitor IV (Boc-Pro-Phe-NHO-Bz-*p*Cl), subtilisin inhibitor V (Boc-Ala-Pro-Phe-NHO-Bz), TIMP-2 (tissue inhibitor of metalloproteinase 2), trypsin inhibitor, secretory leukocyte protease inhibitor, and any mixture there of.

26. The method of claim 24, wherein the agent that alters the activities of G-protein coupled receptors and cAMP or pharmaceutically acceptable derivative is selected from the group consisting of AB-MECA (*N*⁶-4-aminobenzyl-5'-*N*-methylcarboxamidoadenosine), CPA (*N*⁶-cyclopentyladenosine), ADAC (*N*⁶-[4-[[[4-[[[(2-aminoethyl) amino] carbonyl] methyl]-anilino] carbonyl] methyl] phenyl] adenosine), CCPA (2-chloro-*N*⁶-cyclopentyl adenosine), CHA (*N*⁶-cyclohexyladenosine), GR79236 (*N*⁶-[1*S*, *trans*,2-hydroxycyclopentyl] adenosine), *S*-ENBA ((2*S*)-*N*⁶-(2-endonorbanyl)adenosine), IAB-MECA (*N*⁶-(4-amino-3-iodobenzyl)adenosine-

5'-*N*-methylcarboxamidoadenosine), *R*-PIA (*R*-*N*⁶-(phenyl isopropyl) adenosine), ATL146e (4-{3-[6-amino-9-(5-ethylcarbamoyl-3,4-dihydroxy-tetrahydro-furan-2-yl)-9H-purin-2-yl]-prop-2-ynyl}-cyclohexanecarboxylic acid methyl ester), CGS-21680 (APEC or 2-[*p*-(2-carbonyl-ethyl)-phenyl ethyl amino]-5'-*N*-ethylcarboxamidoadenosine), CV1808 (2-phenylaminoadenosine), HENECA (2-hex-1-ynyl-5'-*N*-ethylcarboxamido adenosine), NECA (5'-*N*-ethyl-carboxamido adenosine), PAPA-APEC (2-(4-[2-[(4-aminophenyl)methylcarbonyl]ethyl] phenyl) ethylamino-5'-*N*-ethyl carboxamidoadenosine), DITC-APEC (2-[*p*-(4-isothiocyanatophenylamino thio carbonyl -2-ethyl)-phenylethylamino]-5'-*N*-ethylcarboxamidoadenosine), DPMA (*N*⁶-(2(3,5-dimethoxy phenyl)-2-(2-methylphenyl)ethyl)adenosine), *S*-PHPNECA ((*S*)-2-phenylhydroxypropynyl-5'-*N*-ethylcarboxamidoadenosine), WRC-0470 (2-cyclohexyl methylidenhydrazinoadenosine), AMP-579 (1*S*-[1a,2b,3b,4a(*S*^{*})]]-4-[7-[[2-(3-chloro-2-thienyl)-1-methylpropyl]amino]-3H-imidazo [4,5-*b*] pyridyl-3-yl] cyclopentane carbox amide), IB-MECA (*N*⁶- (3-iodobenzyl)adenosine-5'-*N*-methyluronamide), 2-CIADO (2-chloroadenosine), I-ABA (*N*⁶-(4-amino-3-iodobenzyl) adenosine), *S*-PIA (*S*-*N*⁶-(phenyl isopropyl) adenosine), 2-[(2-aminoethyl-aminocarbonylethyl) phenylethyl amino]-5'-*N*-ethyl-carboxamidoadenosine, 2-Cl-IB-MECA (2-chloro-*N*⁶- (3-iodobenzyl)adenosine-5'-*N*-methyluronamide), adenosine, polyadenylic acid, and any mixture thereof.

27. A method of preventing organ ischemia or reperfusion injury comprising administering to a living subject in need thereof sequentially in any order
 - a. a protease inhibitor; and
 - b. an agent that alters activities of G protein coupled receptors and cAMP or a pharmaceutically acceptable derivative or prodrug thereof.
28. The method of claim 27, wherein the serine protease inhibitor is selected from the group consisting of 4-(2-aminoethyl) benzenesulfonylfluoride, α -amino-*n*-caproic acid, α_1 -antichymotrypsin, antipain, antithrombin III, α_1 -antitrypsin, *p*-amidinophenylmethyl sulfonyl fluoride, aprotinin, cathepsin/subtilisin inhibitor (Boc-Val-Phe-NHO-Bz-*p*Cl), chymostatin ([(*S*)-1-carboxy-2-

phenylethyl]-carbamoyl- \square -[2-amidohexahydro-4(*S*)-pyrimidyl]-(*S*)-glycyl-[A = Leu, B = Val, or C = Ile]-phenylalaninal), chymotrypsin inhibitor I, 3,4-dichloroisocoumarin, diisopropylfluoro phosphate, dipeptidylpeptidase IV inhibitor I (Ile-Pro-Ile), dipeptidylpeptidase IV inhibitor II (H-Glu-(NHO-Bz)-Pyr), ecotin, elastase inhibitor I (Boc-Ala-Ala-Ala-NHO-Bz), \square_2 -macroglobulin, PPACK (*D*-Phe-Pro-Arg-chloromethylketone), PPACK II, *N*^α-tosyl-Lys chloromethyl ketone, *N*^α-tosyl-Phe chloromethyl ketone, acetyl-pepstatin (Ac-Val-Val-(3*S*,4*S*)-Sta-Ala-(3*S*,4*S*)-Sta-OH), calpain inhibitor I (*N*-acetyl-Leu-Leu-norleucinal), calpain inhibitor II (*N*-acetyl-Leu-Leu-Met-CHO), amastatin ([[(2*S*, 2*R*)]-3-amino-2-hydroxy-5-methylhexanoyl]-Val-Val-Asp-OH), arphamenine A ((2*R*,5*S*)-5-amino-8-guanidino-4-oxo-2-phenylmethyl octanoic acid), arphamenine B ((2*R*,5*S*)-5-amino-8-guanidino-4-oxo-2-*p*-hydroxyphenyl methyl octanoic acid), benzamidine, bestatin ([[(2*S*, 2*R*)]-3-amino-2-hydroxy-4-phenyl butanoyl]-*L*-Leucine), CA-074 ((*L*-3-*trans*-[propylcarbamoyl]oxirane-2-carbonyl)-*L*-isoleucyl-*L*-proline), CA-074-Me ((*L*-3-*trans*-[propylcarbamoyl]oxirane-2-carbonyl)-*L*-isoleucyl-*L*-proline-methylester), calpastatin, calpeptin (benzyloxycarbonylleucyl-norleucinal), carboxypeptidase inhibitor, cathepsin inhibitor I (Z-Phe-Gly-NHO-Bz), cathepsin inhibitor II (Z-Phe-Gly-NHO-Bz-*p*Me), cathepsin inhibitor III (Z-Phe-Gly-NHO-Bz-*p*OMe), cathepsin B inhibitor I (Z-Phe-Ala-CH₂F), cathepsin B inhibitor II (Ac-Leu-Val-lysinal), cathepsin L inhibitor I (Z-Phe-Phe-CH₂F), cathepsin L inhibitor II (Z-Phe-Tyr-CHO), cathepsin L inhibitor III (Z-Phe-Tyr-(*t*-Bu)-CHN₂), cathepsin L inhibitor IV (1-naphthalenesulfonyl-Ile-Trp-CHO), cathepsin L inhibitor V (Z-Phe-Tyr(O*t*Bu)-COCHO), cathepsin L inhibitor VI (*N*-(4-biphenylacetyl)-*S*-methylcysteine-(*D*)-Arg-Phe- \square -phenethylamide), cathepsin S inhibitor (Z-Phe-Leu-COCHO), cystatin, diprotin A (H-Ile-Pro-Ile-OH), E-64 (*trans*-epoxysuccinyl-*L*-leucylamido-(4-guanidino)butane), E-64 d (loxistatin, or (2*S*,3*S*)-*trans*-epoxysuccinyl-*L*-leucylamido-3-methylbutane ethyl ester), ebelactone A (3,11-dihydroxy-2,4,6,8,10,12-hexamethyl-9-oxo-6-tetradecenoic 1,3-lactone), ebelactone B (2-ethyl-3,11-dihydroxy-4,6,8,10,12-

penta methyl -9-oxo-6-tetradecenoic 1,3-lactone), EDTA (ethylenediamine tetraacetic acid), EGTA (ethyleneglycol-*bis*(α -aminoethyl)-*N,N,N',N'*-tetraacetic acid), elastase inhibitor II (MeOSuc-Ala-Ala-Pro-Ala-CMK), elastase inhibitor III (MeOSuc-Ala-Ala-Pro-Val-CMK), elastatinal (Leu-(Cap)-Gln-Ala-al or *N*-[(*S*)-1-carboxy-isopentyl]-carbamoyl- α -(2-iminohexahydro-4(*S*)-pyrimidyl)-*L*-glycyl-*L*-glutaminy-*L*-alaninal), E-64 (*trans*-epoxysuccinyl-*L*-leucylamido-(4-guanidino)butane), E-64d (loxistatin, or (2*S*,3*S*)-*trans*-epoxysuccinyl-*L*-leucylamido-3-methylbutane ethyl ester), *N*-ethyl maleimide, GGACK (1,5-dansyl-*L*-glutamyl-*L*-glycyl-*L*-arginine chloro methyl ketone), galardin (*N*-[(2*S*)-(methoxycarbonylmethyl)-4-methylpentanoyl]-*L*-tryptophan-methyl amide), 2-guanidinoethylmercaptosuccinic acid, hirudin, HIV protease inhibitor (Ac-Leu-Val-phenylalaninal), leuhistin (((2*R*,3*S*)-3-amino-2-hydroxy-2-(1*H*-imidazol-4-ylmethyl)-5-methyl)-5-methylhexanoic acid), leupeptin (acetyl-leucyl-leucyl-arginal), NCO-700, PEFABLOC SC (4-(2-aminoethyl)-benzenesulfonyl fluoride), pepstatin (isovaleryl-Val-Val-4-amino-3-hydroxy-6-methylheptanoyl-Ala-4-amino-3-hydroxy-6-methylheptanoic acid), phebestin ((2*S*,3*R*)-3-amino-2-hydroxy-4-phenylbutanoyl-*L*-valyl-*L*-phenylalanine), PMSF (phenyl methyl sulfonyl fluoride), phosphoramidon (*N*- α -*L*-rhamnopyranosyloxy(hydroxyl phosphinyl)-*L*-Leucyl-*L*-tryptophan, plummer's inhibitor (*D,L*-2-mercaptomethyl-3-guanidino-ethylthiopropionic acid), 1,10-phenanthroline, subtilisin inhibitor I (Boc-Ala-Ala-NHO-Bz), subtilisin inhibitor II (Z-Gly-Phe-NHO-Bz), subtilisin inhibitor III (Z-Gly-Phe-NHO-Bz-*p*OMe), subtilisin inhibitor IV (Boc-Pro-Phe-NHO-Bz-*p*Cl), subtilisin inhibitor V (Boc-Ala-Pro-Phe-NHO-Bz), TIMP-2 (tissue inhibitor of metalloproteinase 2), trypsin inhibitor, secretory leukocyte protease inhibitor, and any mixture there of.

29. The method of claim 27, wherein the agent that alters activities of G-protein coupled receptors and cAMP or pharmaceutically acceptable derivative is selected from the group consisting of AB-MECA (*N*⁶-4-aminobenzyl-5'-*N*-methylcarboxamidoadenosine), CPA (*N*⁶-cyclopentyladenosine), ADAC (*N*⁶-

[4-[[[4-[[[(2-aminoethyl) amino] carbonyl] methyl]-anilino] carbonyl] methyl] phenyl] adenosine), CCPA (2-chloro-*N*⁶-cyclopentyl adenosine), CHA (*N*⁶-cyclohexyladenosine), GR79236 (*N*⁶-[1*S*, *trans*,2-hydroxycyclopentyl] adenosine), *S*-ENBA ((2*S*)- *N*⁶-(2-endonorbanyl)adenosine), IAB-MECA (*N*⁶-(4-amino-3-iodobenzyl)adenosine-5'-*N*-methylcarboxamidoadenosine), *R*-PIA (*R*-*N*⁶-(phenyl isopropyl) adenosine), ATL146e (4-{3-[6-amino-9-(5-ethylcarbamoyl-3,4-dihydroxy-tetrahydro-furan-2-yl)-9H-purin-2-yl]-prop-2-ynyl}-cyclohexanecarboxylic acid methyl ester), CGS-21680 (APEC or 2-[*p*-(2-carbonyl-ethyl)-phenyl ethyl amino]-5'-*N*-ethylcarboxamidoadenosine), CV1808 (2-phenylaminoadenosine), HENECA (2-hex-1-ynyl-5'-*N*-ethylcarboxamido adenosine), NECA (5'-*N*-ethyl-carboxamido adenosine), PAPA-APEC (2-(4-[2-[(4-aminophenyl)methylcarbonyl]ethyl] phenyl) ethylamino-5'-*N*-ethyl carboxamidoadenosine), DITC-APEC (2-[*p*-(4-isothiocyanatophenylamino thio carbonyl-2-ethyl)-phenylethylamino]-5'-*N*-ethylcarboxamidoadenosine), DPMA (*N*⁶-(2(3,5-dimethoxy phenyl)-2-(2-methylphenyl)ethyl)adenosine), *S*-PHPNECA ((*S*)-2-phenylhydroxypropynyl-5'-*N*-ethylcarboxamidoadenosine), WRC-0470 (2-cyclohexyl methylidenehydrazinoadenosine), AMP-579 (1*S*-[1a,2b,3b,4a(*S**)])]-4-[7-[[2-(3-chloro-2-thienyl)-1-methylpropyl]amino]-3H-imidazo [4,5-*b*] pyridyl-3-yl] cyclopentane carboxamide), IB-MECA (*N*⁶-(3-iodobenzyl)adenosine-5'-*N*-methyluronamide), 2-CIADO (2-chloroadenosine), I-ABA (*N*⁶-(4-amino-3-iodobenzyl) adenosine), *S*-PIA (*S*-*N*⁶-(phenylisopropyl)adenosine), 2-[(2-aminoethyl-aminocarbonyl)ethyl] phenylethyl amino]-5'-*N*-ethyl-carboxamidoadenosine, 2-Cl-IB-MECA (2-chloro-*N*⁶-(3-iodobenzyl) adenosine-5'-*N*-methyluronamide), adenosine, polyadenylic acid, and any mixture thereof.

30. A method of preventing organ or tissue injury at predetermined point or period of intervention comprising administering to a living subject in need thereof a pharmaceutical composition comprising:
 - a. a protease inhibitor; and
 - b. an agent that alters activities of G protein coupled receptors and

cAMP, an analog or a pharmaceutically acceptable derivative or prodrug thereof.

31. The method of claim 30, wherein the organ or tissue injury is related to at least one of cardiac surgery, non-surgical cardiac revascularization, organ transplantation, perfusion, ischemia, reperfusion, ischemia-reperfusion injury, oxidant injury, cytokine induced injury, shock induced injury, resuscitations injury, or apoptosis.
32. The method of claim 30, wherein the administration is made at the predetermined point of time related to at least one of pre-treatment regimen, pharmacological preconditioning, reperfusion or post interventional therapy, wherein the pharmacological preconditioning is a treatment administered before the ischemic intervention followed by a brief period of reperfusion or washout..
33. The method of claim 30, wherein the protease inhibitor is selected from the group consisting of 4-(2-aminoethyl) benzenesulfonylfluoride, α -amino-*n*-caproic acid, α_1 -antichymotrypsin, antipain, antithrombin III, α_1 -antitrypsin, *p*-amidinophenylmethyl sulfonyl fluoride, aprotinin, cathepsin/subtilisin inhibitor (Boc-Val-Phe-NHO-Bz-*p*Cl), chymostatin ([*(S)*-1-carboxy-2-phenylethyl]-carbamoyl- α -[2-amidohexahydro-4(*S*)-pyrimidyl]-(*S*)-glycyl-[A = Leu, B = Val, or C = Ile]-phenylalaninal), chymotrypsin inhibitor I, 3,4-dichloroisocoumarin, diisopropylfluoro phosphate, dipeptidylpeptidase IV inhibitor I (Ile-Pro-Ile), dipeptidylpeptidase IV inhibitor II (H-Glu-(NHO-Bz)-Pyr), ecotin, elastase inhibitor I (Boc-Ala-Ala-Ala-NHO-Bz), α_2 -macroglobulin, PPACK (*D*-Phe-Pro-Arg-chloromethylketone), PPACK II, *N*^{*α*}-tosyl-Lys chloromethyl ketone, *N*^{*α*}-tosyl-Phe chloromethyl ketone, acetyl-pepstatin (Ac-Val-Val-(3*S*,4*S*)-Sta-Ala-(3*S*,4*S*)-Sta-OH), calpain inhibitor I (*N*-acetyl-Leu-Leu-norleucinal), calpain inhibitor II (*N*-acetyl-Leu-Leu-Met-CHO), amastatin ([*(2S, 2R)*]-3-amino-2-hydroxy-5-methylhexanoyl]-Val-Val-Asp-OH), arphamenine A ((*2R,5S*)-5-amino-8-guanidino-4-oxo-2-phenylmethyl octanoic acid), arphamenine B ((*2R,5S*)-5-amino-8-guanidino-4-oxo-2-*p*-hydroxyphenyl methyloctanoic acid), benzamidine, bestatin ([*(2S,*

2*R*)-3-amino-2-hydroxy-4-phenyl butanoyl] -*L*-Leucine), CA-074 ((*L*-3-*trans*-[propylcarbamoyl]oxirane-2-carbonyl)-*L*-isoleucyl-*L*-proline), CA-074-Me ((*L*-3-*trans*-[propylcarbamoyl]oxirane-2-carbonyl)-*L*-isoleucyl-*L*-proline-methylester), calpastatin, calpeptin (benzyloxycarbonylleucyl-norleucinal), carboxypeptidase inhibitor, cathepsin inhibitor I (Z-Phe-Gly-NHO-Bz), cathepsin inhibitor II (Z-Phe-Gly-NHO-Bz-*p*Me), cathepsin inhibitor III (Z-Phe-Gly-NHO-Bz-*p*OMe), cathepsin B inhibitor I (Z-Phe-Ala-CH₂F), cathepsin B inhibitor II (Ac-Leu-Val-lysinal), cathepsin L inhibitor I (Z-Phe-Phe-CH₂F), cathepsin L inhibitor II (Z-Phe-Tyr-CHO), cathepsin L inhibitor III (Z-Phe-Tyr-(*t*-Bu)-CHN₂), cathepsin L inhibitor IV (1-naphthalenesulfonyl-Ile-Trp-CHO), cathepsin L inhibitor V (Z-Phe-Tyr(O*t*Bu)-COCHO), cathepsin L inhibitor VI (*N*-(4-biphenylacetyl)-*S*-methylcysteine-(*D*)-Arg-Phe-□-phenethylamide), cathepsin S inhibitor (Z-Phe-Leu-COCHO), cystatin, diprotin A (H-Ile-Pro-Ile-OH), E-64 (*trans*-epoxysuccinyl-*L*-leucylamido-(4-guanidino)butane), E-64 d (loxistatin, or (2*S*,3*S*)-*trans*-epoxysuccinyl-*L*-leucylamido-3-methylbutane ethyl ester), ebelactone A (3,11-dihydroxy-2,4,6,8,10,12-hexamethyl-9-oxo-6-tetradecenoic 1,3-lactone), ebelactone B (2-ethyl-3,11-dihydroxy-4,6,8,10,12-penta methyl -9-oxo-6-tetradecenoic 1,3-lactone), EDTA (ethylenediamine tetraacetic acid), EGTA (ethyleneglycol-*bis*(□-aminoethyl)-*N,N,N',N'*-tetraacetic acid), elastase inhibitor II (MeOSuc-Ala-Ala-Pro-Ala-CMK), elastase inhibitor III (MeOSuc-Ala-Ala-Pro-Val-CMK), elastatinal (Leu-(Cap)-Gln-Ala-al or *N*-[(*S*)-1-carboxy-isopentyl]-carbamoyl-α-(2-iminohexahydro-4(*S*)-pyrimidyl]-*L*-glycyl-*L*-glutaminyl-*L*-alaninal), E-64 (*trans*-epoxysuccinyl-*L*-leucylamido-(4-guanidino)butane), E-64d (loxistatin, or (2*S*,3*S*)-*trans*-epoxysuccinyl-*L*-leucylamido-3-methylbutane ethyl ester), *N*-ethyl maleimide, GGACK (1,5-dansyl-*L*-glutamyl-*L*-glycyl-*L*-arginine chloro methyl ketone), galardin (*N*-[(2*S*)-(methoxycarbonylmethyl)-4-methylpentanoyl]-*L*-tryptophan-methyl amide), 2-guanidinoethylmercaptosuccinic acid, hirudin, HIV protease inhibitor (Ac-Leu-Val-phenylalaninal), leuhistin (((2*R*,3*S*)-3-amino-2-hydroxy-2-(1H-

imidazol-4-ylmethyl)-5-methyl)-5-methylhexanoic acid), leupeptin (acetyl-leucyl-leucyl-arginal), NCO-700, PEFABLOC SC (4-(2-aminoethyl)-benzenesulfonyl fluoride), pepstatin (isovaleryl-Val-Val-4-amino-3-hydroxy-6-methylheptanoyl-Ala-4-amino-3-hydroxy-6-methylheptanoic acid), phebestin ((2*S*,3*R*)-3-amino-2-hydroxy-4-phenylbutanoyl-*L*-valyl-*L*-phenylalanine), PMSF (phenyl methyl sulfonyl fluoride), phosphoramidon (*N*-alpha-*L*-rhamnopyranosyloxy(hydroxyl phosphinyl)-*L*-Leucyl-*L*-tryptophan, plummer's inhibitor (*D,L*-2-mercaptomethyl-3-guanidino-ethylthiopropionic acid), 1,10-phenanthroline, subtilisin inhibitor I (Boc-Ala-Ala-NHO-Bz), subtilisin inhibitor II (Z-Gly-Phe-NHO-Bz), subtilisin inhibitor III (Z-Gly-Phe-NHO-Bz-*p*OMe), subtilisin inhibitor IV (Boc-Pro-Phe-NHO-Bz-*p*Cl), subtilisin inhibitor V (Boc-Ala-Pro-Phe-NHO-Bz), TIMP-2 (tissue inhibitor of metalloproteinase 2), trypsin inhibitor, secretory leukocyte protease inhibitor, and any mixture there of.

34. The method of claim 30, wherein the agent that alters activities of G protein coupled receptors and cAMP is selected from the group consisting of AB-MECA (*N*⁶-4-amino benzyl-5'-*N*-methylcarboxamidoadenosine), CPA (*N*⁶-cyclopentyladenosine), ADAC (*N*⁶-[4-[[[4-[[[(2-aminoethyl) amino] carbonyl] methyl]-anilino] carbonyl] methyl] phenyl] adenosine), CCPA (2-chloro-*N*⁶-cyclopentyladenosine), CHA (*N*⁶-cyclohexyladenosine), GR79236 (*N*⁶-[1*S*, *trans*,2-hydroxycyclopentyl] adenosine), *S*-ENBA ((2*S*)- *N*⁶-(2-endonorbanyl)adenosine), IAB-MECA (*N*⁶-(4-amino-3-iodobenzyl)adenosine-5'-*N*-methylcarboxamidoadenosine), *R*-PIA (*R*-*N*⁶-(phenylisopropyl) adenosine), ATL146e (4-{3-[6-amino-9-(5-ethylcarbamoyl-3,4-dihydroxy-tetrahydro-furan-2-yl)-9H-purin-2-yl]-prop-2-ynyl}-cyclohexanecarboxylic acid methyl ester), CGS-21680 (APEC or 2-[*p*-(2-carbonyl-ethyl)-phenyl ethyl amino]-5'-*N*-ethylcarboxamidoadenosine), CV1808 (2-phenylaminoadenosine), HENECA (2-hex-1-ynyl-5'-*N*-ethylcarboxamido adenosine), NECA (5'-*N*-ethyl-carboxamido adenosine), PAPA-APEC (2-(4-[2-[(4-aminophenyl) methyl carbonyl]ethyl] phenyl) ethylamino-5'-*N*-ethyl carboxamidoadenosine), DITC-APEC (2-[*p*-(4-isothiocyanatophenylamino

thiocarbonyl-2-ethyl)-phenylethylamino]-5'-*N*-ethylcarboxamidoadenosine), DPMA (*N*⁶-(2(3,5-dimethoxy phenyl)-2-(2-methyl phenyl) ethyl)adenosine), *S*-PHPNECA ((*S*)-2-phenylhydroxypropynyl-5'-*N*-ethylcarboxamidoadenosine), WRC-0470 (2-cyclohexylmethylidenhydrazinoadenosine), AMP-579 (1*S*-[1a,2b,3b,4a(*S**)]]-4-[7-[[2-(3-chloro-2-thienyl)-1-methylpropyl]amino]-3H-imidazo [4,5-*b*] pyridyl-3-yl] cyclopentane carboxamide), IB-MECA (*N*⁶- (3-iodobenzyl) adenosine -5'-*N*-methyluronamide), 2-CIADO (2-chloroadenosine), I-ABA (*N*⁶-(4-amino-3-iodobenzyl) adenosine), *S*-PIA (*S*-*N*⁶-(phenylisopropyl)adenosine), 2-[(2-aminoethyl-aminocarbonylethyl) phenylethyl amino]-5'-*N*-ethylcarboxamidoadenosine, 2-Cl-IB-MECA (2-chloro-*N*⁶- (3-iodobenzyl)adenosine-5'-*N*-methyluronamide), adenosine, polyadenylic acid, and any mixture thereof.